

Berberamine inhibits the growth of liver cancer cells and cancer-initiating cells by targeting Ca(2+)-calmodulin-dependent protein kinase II.

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Public Summary:

Liver cancer is the third leading cause of cancer deaths worldwide but no effective treatment toward liver cancer is available so far. Therefore, there is an unmet medical need to identify novel therapies to efficiently treat liver cancer and improve the prognosis of this disease. Here, we report that berberamine and one of its derivatives, bbd24, potently suppressed liver cancer cell proliferation and induced cancer cell death by targeting Ca(2+)/calmodulin-dependent protein kinase II (CAMKII). Furthermore, berberamine inhibited the in vivo tumorigenicity of liver cancer cells in NOD/SCID mice and downregulated the self-renewal abilities of liver cancer-initiating cells. Chemical inhibition or short hairpin RNA-mediated knockdown of CAMKII recapitulated the effects of berberamine, whereas overexpression of CAMKII promoted cancer cell proliferation and increased the resistance of liver cancer cells to berberamine treatments. Western blot analyses of human liver cancer specimens showed that CAMKII was hyperphosphorylated in liver tumors compared with the paired peritumor tissues, which supports a role of CAMKII in promoting human liver cancer progression and the potential clinical use of berberamine for liver cancer therapies. Our data suggest that berberamine and its derivatives are promising agents to suppress liver cancer growth by targeting CAMKII. Mol Cancer Ther; 12(10): 2067-77. (c)2013 AACR.

Scientific Abstract:

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